REMARKS

Status of the Claims

Claims 1-15 are pending and under consideration in this application. Claims 1-9 are rejected and claims 10-15 are objected to as being dependent on rejected base claims.

No claims are added or cancelled herein and so, after entry of the amendments made herein, claims 1-15 will be pending and under consideration.

35 U.S.C. § 103(a) rejection

Claims 1-3, 5, 6, and 9 stand rejected as allegedly being unpatentable over Hansbrough et al. Applicants respectfully traverse the rejection.

From the comments on page 4, lines 7-17, of the Office Action, Applicants understand the Examiner's position to be that one of ordinary skill in the art would have considered, based on the disclosure of Hansbrough et al., injecting a fibroblast suspension into a skin burn wound and would have found no teaching in the reference that cells should be used in sheet (rather than injectable) form. Applicants strongly disagree with this position.

Applicants point out that the reference's principal concern is with keratinocytes (see, e.g., page 2125, column 2, lines 15-22; page 2125, column 3, lines 4-20; and page 2127, column 3, line 7, to page 2129, line3) and secondarily refers to the fibroblasts that are used together with the keratinocytes in the compositions it describes. In addition, in the prior Amendment and Response, Applicants provided sound reasons why one of ordinary skill in the art would have been persuaded of the importance of using keratinocytes in sheet form and rather than injecting them into the wound. Those comments are incorporated herein by reference.

Moreover, Hansbrough et al. repeatedly points to its belief that the most important requirement for early skin burn wound treatment is early wound closure or coverage (see, e.g., Abstract, first sentence; introduction section, first and subsequent sentences; Comment section throughout). It is implicit and obvious that early wound closure coverage requires the application to the wound of some sort of sheet or solid structure (e.g., a sheet of cells only, a sheet of matrix material, or a sheet of matrix material with cells attached to it; see, for example,

the introduction section Hansbrough et al.). It is also of course self-evident that injection of a suspension of cells of any type into a wound would not provide the requisite early wound closure or coverage. In this regard, Hansbrough et al. focuses largely on a comparison of its methodology using sheets of matrix material (collagen-glycosaminoglycan; C-CAG) with attached keratinocytes and fibroblasts to other sheet format graft materials (e.g., skin grafts and keratinocyte sheets) (see, e.g., the introduction section; page 2126, last paragraph; page 2127, first and second full paragraphs; and the entire Comment section). Only once, and there only tangentially, does the reference refer to the use of a cell suspension, and in this case, a suspension of keratinocytes (page 2128, last sentence), not fibroblasts. In this and the following sentence it describes the clear advantage of its cell-matrix compositions over such keratinocyte suspensions as well as keratinocyte sheets. Importantly, nowhere does the reference allude to, even remotely suggest, the use of fibroblast suspensions (as required by the present claims).

With respect to the comment on page 4, lines 14-15, of the Office Action, Applicants agree that "[m]any pharmaceutical or bioactive compositions can be given through various formulations." However, as pointed out by Hansbrough et al. and above, injecting keratinocyte suspensions into skin wounds would at the priority date of the present application have been considered by those ordinarily skilled in the art far less likely to successful than placement of cell-matrix composites such as those described in the reference and therefore not obvious to do. Most importantly, as indicated above, Hansbrough et al. does not mention of even suggest the possibility of using fibroblast suspensions. Finally, the question posed on page 4, lines 16-17, of the Office Action ("[W]hat is the criticality of the suspension over the sheet of Hansbrough et al?") is answered by Hansbrough et al. itself and the above discussion of the reference.

In light of the above considerations, one of ordinary skill in the art would not have considered it obvious, based on the disclosure of Hansbrough et al., to inject a suspension of any cells (e.g., keratinocytes), let alone fibroblasts, into a burn wound. Moreover, if such an artisan had previously considered doing so, the teachings of Hansbrough et al. would have dissuaded him or her and persuaded him or her to rather use the cell-matrix composite it describes.

Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 103 (a) be withdrawn.

35 U.S.C. § 102(b) rejection

Claims 1-9 stand rejected as allegedly being anticipated by DE 197 16 098 (DE'098). Applicants respectfully traverse the rejection.

From the comments on page 5, lines 1-3, of the Office Action, Applicants understand the Examiner's position to be that DE'098 discloses "culturing in the subjects serum." Applicants have looked carefully at the text of the reference specifically cited by the Examiner, i.e., page 2, lines 22-25 and claims 1 and 12 (but not "page 4, column 17" which does not exist the document) and the entire document. While not being proficient in the German language, Applicants can find no language that appears to disclose, or even suggest, culturing cells in a subject's own serum. In addition, Applicants have read English language U.S. Application Serial No. 09/402,840 (the '840 application), Canadian Application No. 2,286,548, and Australian Application No. 1998-072150, all of which appear to be national phase applications of International Application No. PCT/EP98/02038 of which DE'098 is a priority document. Applicants can find no disclosure or suggestion in the three English language documents referred to above of culturing cells in a subject's own serum. Applicants respectfully request the Examiner to point to the particular text of DE'098 that he believes to make this disclosure.

Moreover, Applicants can find no other text in DE'098 (or the apparently corresponding English language applications) that directly or inherently disclose "culturing the fibroblasts in a culture medium such that the cultured fibroblasts are non-immunogenic when administered" (as required by claim 1). Citations to the disclosure of DE'098 below are actually to the U.S. application referred to above (the '840 application). By comparing the relevant text, Applicants believe that in all cases, the corresponding text of DE'098 has the same meaning as that of the relevant text of the '840 application. For the convenience of the Examiner, a copy of the '840 application is enclosed as Exhibit A.

As is made abundantly clear throughout the '840 application, fibroblasts are used in its methods principally as factories of recombinant factors encoded by foreign genes with which they are transfected. Moreover, as indicated on page 5, lines 28-37, of the '840 application, in a particularly preferred embodiment of the invention, the foreign gene-transfected cells are irradiated prior to administration so that they die in the body after a very short time.

Furthermore, the document states that while the gene-transfected fibroblasts can be autologous (i.e., from the subject), they are preferably allogeneic (i.e., obtained from another individual) (page 5, lines 20-24). This is in contrast to the untransfected keratinocytes that the '840 application indicates can also be administered to the subject and which are *per se* (rather than foreign gene products as in the case of transfected fibroblasts) therapeutic agents; these keratinocytes are preferably autologous (page 4, line 38, to page 5, line 3).

Overall, DE'098 teaches that it is generally desirable for its foreign gene-transfected cells to persist in a host subject for only a short length of time and thus there is no need for such cells to have low immunogenicity so as to avoid the possibility of them eliciting an immune response in the host subject and then be rejected by the subject. Indeed, one of ordinary skill in the art reading DE'098 would, based on the above-mentioned preference for allogeneic over autologous fibroblasts, consider it desirable for the foreign gene-transfected fibroblasts to be immunogenic precisely for this reason.

Thus, Applicants respectfully submit that not only does DE'098 fail to explicitly teach culturing fibroblasts in a culture medium such that the cultured fibroblasts are non-immunogenic when administered, it does not inherently do so either. Indeed, as pointed out above, it teaches quite the opposite, i.e., that gene-transfected fibroblasts are preferably immunogenic by virtue of being allogeneic.

In view of these considerations, Applicants respectfully submit that DE'098 does not directly or inherently disclose each and every element of the claims at issue and therefore request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

CONCLUSION

In summary, in view of the amendments and remarks set forth above, Applicants request that the Examiner permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' undersigned representative can be reached at the telephone number below.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 10592-023US1.

Respectfully submitted,

Date: 6/19/09

/Stuart Macphail/

Stuart Macphail, Ph.D., J.D.
Reg. No. 44,217

Fish & Richardson P.C.
Citigroup Center
52nd Floor
153 East 53rd Street
New York, New York 10022-4611
Telephone: (212) 765-5070
Facsimile: (877) 769-7945